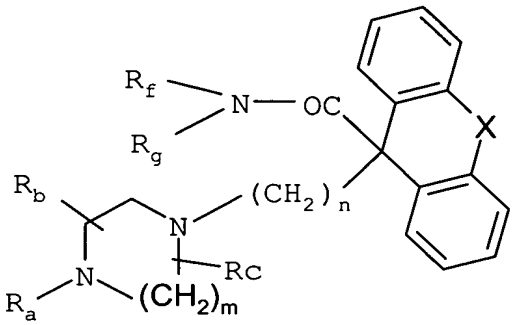
Docket no. 5/1272US

CLEAN SET OF NEW CLAIMS

--11 (New). A compound of the formula (I)



, (I)

wherein

n denotes the number 1, 2, 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond, an oxygen atom, a methylene, ethylene, imino or N-(C_{1-3}-alkyl)-imino group,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R_1 and R_2, wherein

> R_1 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a phenoxy, heteroaryloxy, phenyl-C_{1-3}-alkoxy, carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkyl-aminocarbonyl, N,N-di-(C_{1-3}-alkyl)-aminocarbonyl, nitro, amino, C_{1-3}-alkylamino,

di-(C_{1-3}-alkyl)-amino, phenyl-C_{1-3}-alkyl-amino, N-(C_{1-3}-alkyl)-phenyl-C_{1-3}-alkylamino, C_{1-3}-alkylcarbonylamino, N-(C_{1-3}-alkyl)-C_{1-3}-alkylcarbonylamino, C_{1-3}-alkylsulphonylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkylsulphonylamino group, wherein the abovementioned phenyl or heteroaryl moieties of the group R_1 are optionally substituted by one to five fluorine, chlorine or bromine atoms, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, and

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or

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R_1 and R_2 together represent a methylenedioxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl or monocyclic heteroaryl group, while the abovementioned phenyl groups and heteroaryl groups are optionally in each case substituted by a fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by a hydroxy, C_{1-3}-alkoxy, carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkylaminocarbonyl or N,N-di-(C_{1-3}-alkyl)-aminocarbonyl group,

R_b and R_c independently of one another denote a hydrogen atom or a C_{1-3}-alkyl group and

R_f and R_g, which are identical or different, denote hydrogen atoms, C_{1-6}-alkyl groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, C_{3-7}-cycloalkyl groups, phenyl, heteroaryl, phenyl-C_{1-3}-alkyl or heteroaryl-C_{1-3}-alkyl groups, while the abovementioned phenyl groups and heteroaryl groups are optionally in each case be substituted by one to three fluorine, chlorine or bromine atoms, by one to

three C_{1-3}-alkyl groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C_{1-3}-alkoxy groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or by a carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, N,N-di-(C_{1-3}-alkyl)-aminocarbonyl, N,N-di-(C_{1-3}-alkyl)-amino, nitro or amino group, or

R_f and R_g together with the nitrogen atom between them denote a 3- to 7-membered cycloalkyleneimino group, while the methylene group in the 4 position of a 6- or 7-membered cycloalkyleneimino group is optionally replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N-(C_{1-3}-alkyl)-imino group,

wherein the tricyclic group in the abovementioned formula I are mono- or disubstituted by fluorine or chlorine atoms, by methyl or methoxy groups and the substituents are identical or different,

and wherein the abovementioned heteroaryl groups in this claim are 6-membered heteroaryl groups containing one, two or three nitrogen atoms, or 5-membered heteroaryl groups containing one to four heteroatoms selected from nitrogen, oxygen and sulphur, while hydrogen atoms bound to nitrogen is optionally replaced by C_{1-3}-alkyl groups,
or
the isomers or the salts thereof.

12 (New). The compound according to claim 11, wherein

n denotes the number 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond, an oxygen atom, a methylene, ethylene, imino or N-(C_{1-3}-alkyl)-imino group,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R_1 and R_2, wherein

R_1 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a phenoxy, heteroaryloxy, phenyl-C_{1-3}-alkoxy, carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, N,N-di-(C_{1-3}-alkyl)-aminocarbonyl, nitro, amino, C_{1-3}-alkylamino, di-(C_{1-3}-alkyl)-amino, phenyl-C_{1-3}-alkyl-amino, N-(C_{1-3}-alkyl)-phenyl-C_{1-3}-alkylamino, C_{1-3}-alkylcarbonylamino, N-(C_{1-3}-alkyl)-C_{1-3}-alkylcarbonylamino, C_{1-3}-alkylsulphonylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkylsulphonylamino group, wherein the abovementioned phenyl or heteroaryl moieties of the group R_1 are optionally substituted by one to five fluorine, chlorine or bromine atoms, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, and

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R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or

R_1 and R_2 together represent a methylenedioxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl or monocyclic heteroaryl group, wherein the abovementioned phenyl groups and heteroaryl groups are optionally in each case be substituted by a fluorine, chlorine or

bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by a hydroxy or C_{1-3}-alkoxy group,

R_b and R_c independently of one another denote a hydrogen atom or a C_{1-3}-alkyl group and

R_f and R_g, which are identical or different, denote hydrogen atoms, C_{1-6}-alkyl groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, C_{3-7}-cycloalkyl groups, phenyl, heteroaryl, phenyl-C_{1-3}-alkyl or heteroaryl-C_{1-3}-alkyl groups, wherein the abovementioned phenyl groups and heteroaryl groups are optionally in each case be substituted by one to three fluorine, chlorine or bromine atoms, by one to three C_{1-3}-alkyl groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C_{1-3}-alkoxy groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or by a carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, N,N-di-(C_{1-3}-alkyl)-aminocarbonyl, N,N-di-(C_{1-3}-alkyl)-amino, nitro or amino group, or and

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R_f and R_g together with the nitrogen atom between them denote a 3- to 7-membered cycloalkyleneimino group, wherein the methylene group in the 4 position of a 6- or 7-membered cycloalkyleneimino group is optionally replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N-(C_{1-3}-alkyl)-imino group.

13. The compound according to claim 11, wherein

n denotes the number 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond or an oxygen atom,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R_1 and R_2, wherein

R_1 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a phenoxy, heteroaryloxy, phenyl-C_{1-3}-alkoxy, carboxy, C_{1-3}-alkoxycarbonyl, aminocarbonyl, C_{1-3}-alkylaminocarbonyl, N,N-di-(C_{1-3}-alkyl)-aminocarbonyl, nitro, amino, C_{1-3}-alkylamino, di-(C_{1-3}-alkyl)-amino, phenyl-C_{1-3}-alkyl-amino, N-(C_{1-3}-alkyl)-phenyl-C_{1-3}-alkylamino, C_{1-3}-alkylcarbonylamino, N-(C_{1-3}-alkyl)-C_{1-3}-alkylcarbonylamino, C_{1-3}-alkylsulphonylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkylsulphonylamino group, wherein the abovementioned phenyl or heteroaryl moieties of the group R_1 are optionally substituted by one to five fluorine, chlorine or bromine atoms, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a hydroxy group, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, and

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or a C_{1-4}-alkoxy group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or

R_1 and R_2 together represent a methylenedioxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl or monocyclic heteroaryl group, wherein the abovementioned phenyl groups and heteroaryl groups are optionally in each case be substituted by a fluorine, chlorine or bromine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by a hydroxy or C_{1-3}-alkoxy group,

R_b and R_c independently of one another denote a hydrogen atom or a methyl group and

R_f denotes a hydrogen atom, a C_{1-6}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a C_{3-7}-cycloalkyl group, phenyl, heteroaryl, phenyl-C_{1-3}-alkyl or heteroaryl-C_{1-3}-alkyl group, while the abovementioned phenyl groups and heteroaryl groups are optionally in each case be substituted by one to three fluorine, chlorine or bromine atoms, by one to three C_{1-3}-alkyl groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C_{1-3}-alkoxy groups wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, or by a nitro or amino group, and

R_g denotes a hydrogen atom.

14(New). The compound according to claim 11, wherein

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n denotes the number 4,
m denotes the number 2,

X denotes a carbon-carbon bond or an oxygen atom,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R_1 and R_2, wherein

> R_1 denotes a hydrogen, fluorine or chlorine atom, a C_{1-3}-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a C_{1-4}-alkoxy group, a phenoxy group, a phenyl-C_{1-3}-alkoxy or a nitro or amino group,
>
> wherein the abovementioned phenyl moiety of the phenoxy group is optionally substituted by a chlorine atom or by a methoxy group,

R_2 denotes a hydrogen atom, a chlorine atom or a C_1-C_4-alkoxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl group,

R_b and R_c independently of one another denote a hydrogen atom or a C_{1-3}-alkyl group and

R_f denotes a C_1-C_6-alkyl group wherein the hydrogen atoms are optionally wholly or partly replaced by fluorine atoms, a phenyl-C_{1-3}-alkyl group, while the abovementioned phenyl group is optionally substituted in each case by a fluorine atom or by a C_1-C_3-alkoxy group, and

R_g denotes a hydrogen atom.

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15(New). A compound chosen from

9-[4-(4-biphenyl-3-yl-piperazin-1-yl)-butyl]-9H-fluorene-9-carboxylic acid-(2,2,2-trifluoroethyl)-amide and

9-[4-(4-biphenyl-4-yl-piperazin-1-yl)-butyl]-9H-fluorene-9-carboxylic acid-(2,2,2-trifluoroethyl)-amide

or the isomers and the salts thereof.

16(New). A physiologically acceptable salt of the compound according to claim 11.

17(New). A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claim 11 with one or more pharmaceutically acceptable inert carriers and/or diluents.

18(New). A method of a lowering plasma levels of atherogenic lipoproteins in a patient, said method comprising administering to a patient in need thereof a pharmaceutically effective amount of a compound according to claim 11.

19(New). A method of treating a disease selected from hyperlipidaemias, atherosclerosis and the clinical sequela thereof, diabetes mellitus, adiposity and pancreatitis, said method comprising administering to a patient in need thereof a pharmaceutically effective amount of a compound according to claim 11.

20(New). The method according to either of claims 18 or 19 wherein the compound according to claim 11 is combined with another lipid-lowering agent.

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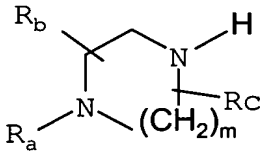
21(New). Process for preparing a compound of the formula (I) according to claim 1, comprising

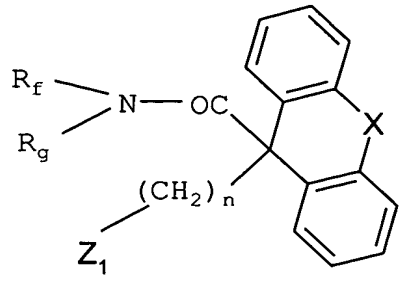
a) reacting under suitable conditions a compound of formula



, (II)

wherein

R_a, R_b and R_c are defined as in claims 1, with a compound of formula



, (III)

wherein

n, R_f, R_g and the tricyclic system are defined as in claims 1 and

Z_1 denotes a nucleofugic leaving group, or

b) reacting under suitable conditions a compound of formula

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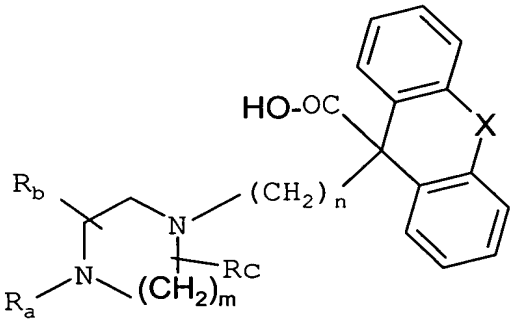
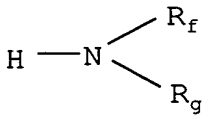


, (IV)

wherein

the tricyclic system is defined as in claims 1, with an amine of formula



, (V)

wherein

R_f and R_g are defined as in claims 1, or with the reactive derivatives thereof and

c) optionally reducing under suitable conditions the product of a) or b) which contains a nitro group if desired into a corresponding amino compound and/or

d) if R_f denotes a hydrogen atom alkylating under suitable conditions the product into a corresponding compound wherein R_f denotes a C_{1-3}-alkyl or phenyl-C_{1-3}-alkyl group, and/or

e) cleaving under suitable conditions any protecting group using to protect reactive groups during the reactions and/or

resolving the product any of the product above into its stereoisomers and/or

converting any of the products above into the physiologically acceptable salts thereof.--